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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,273	08/27/2003	Jian Chen	D0073 CNT	7258

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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SWOPE	
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1656	0206

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Commissioner for Patents

Please find enclosed a copy of the First Action on the Merits of this case mailed February 2, 2006, signed by the director, as required by MPEP 1003 [R-2].

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER

Office Action Summary	Application No.	Applicant(s)	
	10/649,273	CHEN ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-64* is/are rejected.

7)☐ Claim(s) *50-52,59,60 and 62* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 33-64 are pending. Said claims encompass a single invention directed to a nucleic acid molecule encoding the polypeptide of SEQ ID NO: 2 and variants thereof, class 536, subclass 23.2. Claims 33-64 are hereby examined.

Priority

The priority date of the invention is taken to be August 27, 2003, the filing date of the instant application. Provisional applications US 60/266,518, filed February 5, 2001, and US 60/282,814, filed April 10, 2001, fail to disclose a nucleic acid molecule encoding a polypeptide having at least 95.0% homology to SEQ ID NO: 2 or fragments thereof.

Specification-Objections

The specification is objected to for not stating, in the first sentence, that parent application 10/067,443 has issued.

The specification is objected for failing to refer to all of the sequences disclosed in the sequence listing. The sequence listing discloses 71 sequences. The specification fails to refer to SEQ ID NOs: 33-40, 42-59, and 60-68.

The specification is objected to for failing to describe, in the figure legends, all of the sequences represented in the drawings. Figure 6 discloses six sequences, three protein sequences and three nucleic acid sequences; but, the legend for Figure 6 only provides sequence identifier numbers for two sequences. Likewise, Figure 7 discloses six sequences, three protein sequences and three nucleic acid sequences; but, the legend for Figure 7 only provides sequence identifier numbers for two sequences. Correction is required.

The specification is objected to for referring to SEQ ID NO: 1 as a polypeptide. See, for example, on page 78. It is requested that the complete Application be carefully check and corrections made.

Abstract

The abstract is objected to for having an abbreviation, MP-1, that is not defined and for using the legal term "said" on line 3.

Claims-Objections

The claim set is objected to for inconsistent formatting for the word claim, wherein in some instances "claim" is used and in other instances "Claim" is used.

Claim 60 is object to for being redundant with Claim 48.

Claims 50-52, 59, and 62 are objected to for improper antecedent usage as follows.

For Claim 50, "The isolated polynucleotide of claim 33" should be "The isolated nucleic acid molecule of claim 33", while "said nucleic acid sequence" should be "said polynucleotide". Claims 51 and 52 are objected to for the same reasons.

For Claim 59, "the vector sequences of claim 58" should be "the vector of claim 58".

For Claim 62, "said nucleic acid sequence" should be "said nucleic acid molecule".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Claims 33-64 are rejected under 35 U.S.C. §101 because the claimed invention lacks patentable utility. The specification fails to teach a specific and substantial function for the

polynucleotide of SEQ ID NO: 1, or any polynucleotide that encodes the protein set forth by SEQ ID NO: 2. Based on the title of the instant invention, the asserted utility for said protein is as a metalloprotease. However, as acknowledged by Applicants (pg 3-5), the family of metalloprotease is a large and variable family of enzymes with a large number of variable substrates and the potentiality of being involved in many different cellular processes and diseases (Massova et al, 1998). Thus, the specification fails to assert a specific and substantial utility for the protein of SEQ ID NO: 2. Furthermore, a specific and substantial function for the protein of SEQ ID NO: 2, as a metalloprotease, is not taught by either the specification or the prior art. Neither the specification nor the prior art teach the substrates cleaved by the recited protein, specific cellular process mediating by said protein, or a specific disease that the disclosed protein, or any encoding polynucleotide, is involved in.

A utility for the protein of SEQ ID NO: 2 as a metalloprotease cannot be deduced based on homology to any protein with a well-established function. Fig 8 shows the level of sequence homology for the polypeptide of SEQ ID NO: 2 with a series of proteins annotated as proteases. The level of homology ranges between 22.5% and 41%. A person of ordinary skill in the art would not be convince, based solely on this level of identity, that the protein of SEQ ID NO: 2 is a metalloprotease. Moreover, none of the proteins listed in Fig 8 have been demonstrated to have metalloprotease activity or any other type of protease activity or, in fact, any enzymatic activity. Furthermore, sequence searches did not reveal the protein of SEQ ID NO: 2 as having significant homology to any protein with demonstrated protease activity or any other kind of enzymatic activity. Therefore, a utility of the protein set forth by SEQ ID NO: 2, as a metalloprotease, cannot be deduced based on homology to any protein having a well-established function.

Without knowing the substrates cleaved by the recited protein, specific cellular process mediating by said protein, or a specific disease in which the protein of SEQ ID NO: 2 is involved, the skilled artisan would not know how to use said protein or the polynucleotide encoding it. Mere assertion that the protein is a metalloprotease does not provide a specific and substantial utility.

The specification (pg 31) also asserts that, based on the expression profile, the nucleic acid molecule of SEQ ID NO: 1, which encodes the polypeptide of SEQ ID NO: 2, would be useful in diagnostic methods for identifying patients with the juvenile form of amyotrophic lateral sclerosis (ALS2). However, the gene encoding MP-1 is not specific for ALS2. The art teaches that the gene for ALS2, *alsin*, is located at 2q33 and the structure of the encoded protein, Alsin, predicts it to be a guanine nucleotide exchange factor, not a metalloprotease (Kunst et al, 2004; pg 937-38). The art also teaches that Alsin regulates the GTPase activity of Rac, thereby stimulating neurite outgrowth (Tudor et al, 2005; Fig 1 & 5). Although the gene for MP-1 is at a neighboring loci to the *alsin* gene, the gene for MP-1 would not have a patentable utility for mapping of ALS2, since the gene for ALS2 is already mapped. Furthermore, the mutations in the alsin gene that cause ALS2 are known (Yang et al, 2001); therefore, the skilled artisan would not find analysis of the MP-1 gene useful for diagnosis of ALS.

For these reasons Claims 33-64 are rejected under 35 U.S.C. §101 because the claimed invention lacks a specific, substantial and credible patentable utility.

Claims 33-64 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 33-64 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-24 of US Patent 6,642,041. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 33-64 herein and Claims 1-24 of 6,642,041 are both directed to nucleic acid molecules encoding the protein of SEQ ID NO: 2 herein and fragments thereof. The claims differ in that Claims 33-64 herein also recite nucleic acid molecules encoding variants of SEQ ID NO: 2 and variants of fragments of SEQ ID NO: 2, wherein the variant has at least 95% homology. The portion of the specification in 6,642,041 that supports the recited nucleic acid molecules would anticipate Claims 33-64 herein, e.g., nucleic acid molecules encoding the protein of SEQ ID NO: 2 and fragments thereof. Claims 33-64 herein cannot be considered patentably distinct over Claims 1-24 of 6,642,041 when there are specifically recited embodiments, (nucleic acid molecules

encoding the protein of SEQ ID NO: 2 and fragments thereof) that would anticipate Claims 33-64 herein. Alternatively, Claims 33-64 herein cannot be considered patentably distinct over Claims 1-24 of 6,642,041 when there are specifically disclosed embodiments in 6,642,041 that supports Claims 1-24 of that patent and falls within the scope of Claims 33-64 herein, because it would have been obvious to a skilled artisan to select nucleic acid molecules of Claims 1-24 of 6,642,041 that anticipate the instant invention, by selecting a specifically disclosed embodiment that supports those claims, i.e., a nucleic acid molecule encoding the protein of SEQ ID NO: 2 and fragments thereof, as disclosed in 6,642,041. One having ordinary skill in the art would have been motivated to do this, because such an embodiment, is disclosed as being a preferred embodiment within the claims of the prior patent.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 33 and 39 recite the cDNA clone contained in ATCC Deposit No: PTA-2766 and a variant thereof, respectively. The specification states that "A representative clone containing all or most of the sequence for SEQ ID NO: 1 was deposited with the American Type Culture Collection ("ATCC"). As shown in Table I, each clone is identified by a cDNA clone ID..." (pg 21, lines 10-12). Table I presents PTA-2766 as comprising SEQ ID NO: 1 and having 2197 nucleic acid residues (pg 63). It is not clear from this whether PTA-2766 is the exact sequence of SEQ ID NO: 1 or, alternatively, contains all or most of the sequence for

SEQ ID NO: 1. The skilled artisan would not know the metes and bounds of the recited invention. Thus, Claims 33 and 39 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 33, 36-38, 43, 47, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al, 2000. Chen et al teach a polynucleotide comprising a coding sequence for a polypeptide having 98% homology to residues 148-414 of SEQ ID NO: 2 and 98% homology to residues 176-414 of SEQ ID NO: 2. Therefore, Claims 33, 36-38, 43, 47, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al, 2000.

Claims 33-40, 46-51, 60, and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by Gandhi et al, 2005 (priority date 13-JUL-2001; US 60/305,405). Gandhi et al teach a polynucleotide that encodes the polypeptide of SEQ ID NO: 2. Gandhi et al also teach recombinant production of their encoded protein, wherein the polynucleotide can also comprise a coding sequence for a heterologous peptide. Therefore, Claims 33-40, 46-51, 60, and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by Gandhi et al, 2005.

Claims 33-40, 46-50, and 60 are rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg et al, 2002. Strausberg et al teach a vector comprising a polynucleotide that encodes the polypeptide of SEQ ID NO: 2. Therefore, Claims 33-40, 46-50, and 60 are rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg et al, 2002.

Claims 33, 36-38, 40, 46-50, 51, and 60 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al, 2004 (filing date 30-JAN-2001). Tang et al, 2004 teach a polynucleotide, SEQ ID NO: 177 therein, comprising a coding sequence for residues 75-414 of SEQ ID NO: 2 herein. Tang et al teach recombinant production of their encoded protein, wherein the polynucleotide can also comprise a coding sequence for a heterologous peptide. Therefore, Claims 33, 36-38, 40, 46-50, 51, and 60 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al, 2004.

Examiner's note: Claims 48 and 60, which recite a host cell expressing a sequence provided as SEQ ID NO: 2 reads on a host cell expressing any fragment of SEQ ID NO: 2. It is suggest that "a sequence provided as SEQ ID NO: 2" be amended to "the sequence provided as SEQ ID NO: 2".

Claims 33-38, 46, 47, 49-52 are rejected under 35 U.S.C. 102(e) as being anticipated by Leiby et al, 2003 (priority date 08-NOV-2000). Leiby et al teach at polynucleotide encoding a polypeptide having 98% homology with SEQ ID NO: 2. The polynucleotide of Leiby et al also encodes a polypeptide having 97% homology with residues 148-414 of SEQ ID NO: 2 and 97% homology with residues 176-414 of SEQ ID NO: 2. Leiby et al teach recombinant production of their encoded protein, wherein the polynucleotide can also comprise a coding sequence for a heterologous peptide, including the Fc domain. Therefore, Claims 33-38, 46, 47, 49-52 are rejected under 35 U.S.C. 102(e) as being anticipated by Leiby et al, 2003.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al, 2000 in view of Tsuruta et al., 1999, Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gandhi et al, 2005 in view of Tsuruta et al., 1999, and Claims 51, 52, 60, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strausberg et al, 2002 in view of Tsuruta et al., 1999. The teachings of Chen et al and Gandhi et al are described above. Neither Chen et al, Gandhi et al, nor Strausberg et al teach a fusion protein comprising their protein linked to the Fc domain. However, fusion proteins comprising the Fc domain are well known in the art. For example, Tsuruta et al teach a fusion protein comprising vascular cell adhesion molecule linked to the Fc domain. It would have been obvious to a person of ordinary skill in the art to use the method of Tsuruta et al to prepare a fusion protein comprising the protein of Chen et al, Gandhi et al, or Strausberg et al and the Fc domain. Motivation to do so is provided by the fact that the Fc domain provides a tag for purification and localization of said proteins. The expectation of success is high, as Fc-linked fusion proteins are well known in the art. Therefore, Claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al, 2000 in view of Tsuruta et al., 1999, Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gandhi et al, 2005 in view of Tsuruta et al., 1999, and Claims 51, 52,

60, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strausberg et al, 2002 in view of Tsuruta et al., 1999.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, and requests for extension of time be submitted on separate pages.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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